UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/523,114	08/02/2005	Francois-Xavier Jacques Berthet	B45314	4557

23347 7590 08/20/2009

GLAXOSMITHKLINE
CORPORATE INTELLECTUAL PROPERTY, MAI B482
FIVE MOORE DR., PO BOX 13398
RESEARCH TRIANGLE PARK, NC 27709-3398

EXAMINER	
ARCHIE, NINA	

ART UNIT	PAPER NUMBER
1645	

NOTIFICATION DATE	DELIVERY MODE
08/20/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

USCIPRTP@GSK.COM
LAURA.M.MCCULLEN@GSK.COM
JULIE.D.MCFALLS@GSK.COM

Office Action Summary	Application No.	Applicant(s)	
	10/523,114	BERTHET ET AL	
	Examiner	Art Unit	
	Nina A. Archie	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *4/1/2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-57 and 60-71* is/are pending in the application.

4a) Of the above claim(s) *9-12,20-44,48-50,56,57 and 60-71* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8,13-19,45-47 and 51-55* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. This Office is responsive to Applicant's response filed 4-1-09. Claims 1-57, 60-71 are pending. Claims 9-12, 20-44, 48-50, 56-57, and 60-71 are withdrawn from consideration. Claims 1-8, 13-19, 45-47, and 51-55 are under examination.

Rejections Withdrawn

2. In view of the Applicant's amendment and remark the following rejections are withdrawn.

a) The rejection of claims 1-8, 13-19, 45, 47, and 51-55 under 35 U.S.C. 102(a) as being by Hermand et al WO 02/30458A1 April 18, 2002 is withdrawn in view of Applicant's arguments.

Double Patenting Rejection Maintained

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

3. The rejection of claims 1-8, 13-19, 45-47, 51-53, and 55 on the grounds of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-17, 19-45, 52-61, 93-113 of copending Application No. 10/523,117 is maintained for the reasons set forth in the previous office action.

Examiner notes that Applicants state the rejection be held in abeyance until the claims of one of the patent applications are found to be allowable.

Claim Rejections Maintained - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. The rejection of claims 1-8, 13-19, 45-47, 51-55 under 35 U.S.C. 102(b) as being by Berthet et al WO/2001/009350 February 8, 2001 are maintained for the reasons set forth in the previous office action.

Applicant arguments:

Applicants arguments filed in response to the 35 U.S.C. 102(b), April 4, 2009 is carefully considered, but not found to be persuasive for the reasons below.

Applicants argue Berthet et al. do not teach an immunogenic composition comprising an isolated transferrin binding protein (Tbp) or antigenic fragment thereof and an isolated Hsf like protein or antigenic fragment thereof from the same or different Gram negative bacteria, as recited in Applicants' independent Claim 1. In contrast, Berthet et al. relates to "an immuno-protective and non-toxic Gram-negative bleb vaccine suitable for pediatric use….The blebs of the invention are improved by one or more genetic changes to the chromosome of the bacterium, including up-regulation of protective antigens, down-regulation of immunodominant non-protective antigens, and detoxification of the Lipid A moiety of LPS." (Abstract, emphasis added). Each of the methods described by Berthet et al. relates to methods to effectuate changes in the antigen expression in blebs. Berthet et al. do not describe each and every element as set forth in Applicants' independent Claim 1. Berthet et al. do not teach an immunogenic composition comprising isolated transferrin binding protein (Tbp) or antigenic fragment thereof and an isolated Hsf like protein or antigenic fragment thereof from the same or different Gram negative bacteria.

Examiner's Response to Applicant's Arguments:

In response to applicant's statement as set forth supra, the claims are drawn to an immunogenic composition comprising an isolated transferring binding protein (Tbp) or antigenic fragment thereof and an isolated Hsf like protein or antigenic fragment thereof

from the same or different Gram negative bacteria. The specification defines Hsf like proteins as autotransporter proteins sharing homology with Hsf of N. meningitidis with the sequences found in WO99/31132; preferably sharing over 40%, 50%, 60%, 70%, more preferably over 80%, most preferably over 90%, most preferably over 95%, 96%, 97%, 98%, 99% identity with an Hsf amino acid sequence found in WO99/31132 (preferably SEQ ID NO 2,4,6 or 8).

Berthet et al teach a bleb vaccine comprising a genetically-engineered bleb preparation isolated from a modified *Nesseria* strain wherein one ore more genes are upregulated such as Hsf-like, TbpA, and TbpB antigens (see claims 1-2, 13-14) wherein the Gram-negative bacterial strain such as *N. meningitidis B* strain is characterized in that said preparation is obtainable by employing one or more processes such as a process of upregulating expression of protective OMP antigens within the bleb preparation comprising the steps of identifying such antigen, engineering a bacterial strain so as to introduce a stronger promoter sequence upstream of a gene encoding said antigen such that said gene is expressed at a level higher than in the non-modified bleb, and making blebs from said strain or a process of upregulating expression of protective OMP antigens within the bleb preparation comprising the steps of identifying such antigen, engineering a bacterial strain so as to introduce into the chromosome one or more further copies of a gene encoding said antigen controlled by a heterologous, stronger promoter sequence, and making blebs from said strain (see claims 1 and 2) which correlate to an immunogenic composition an immunogenic composition comprising an isolated transferring binding protein (Tbp) or antigenic fragment thereof and an isolated Hsf like protein or antigenic fragment thereof from the same or different Gram negative bacteria. Therefore Berthet et al teaches a an immunogenic composition comprising antigens Hsf-like and TbpA and TbpB.

Although Berthet et al teach methods to effectuate changes in the antigen expression in blebs the claims encompass an immunogenic composition comprising a Tbp antigenic fragment thereof and an Hsf like antigenic fragment thereof thus Berthet et al meet the limitations to the claims.

As outlined previously, the claims are drawn to an immunogenic composition comprising an isolated transferring binding protein (Tbp) or antigenic fragment thereof and an isolated Hsf like protein or antigenic fragment thereof from the same or different Gram negative bacteria (claim 1), wherein the transferrin binding protein or fragment thereof and Hsf like protein or fragment thereof are from Neisseria (claim 2), wherein the transferrin binding protein or fragment thereof is derived from N. meningitidis (claim 3), wherein the Hsf like protein or fragment thereof is derived from N. meningitidis (claim 4), wherein the transferrin binding protein or fragment thereof is derived from N. meningitidis serogroup B (claim 5), wherien the Hsf like protein or fragment thereof is derived from N. meningitidis serogroup B (claim 6), wherein the transferrin binding protein or fragment thereof is derived from N. gonorrhoeae (claim 7), wherein the Hsf like protein or antigenic fragment thereof is derived from N. gonorrhoeae (claim 8), wherein the transferrin binding protein is TbpA or an antigenic fragment thereof (claim 13), comprising high molecular weight form TbpA or low molecular weight form TbpA or both high molecular weight form TbpA and low molecular weight form TbpA (claim 14), wherein the Hsf like protein is Hsf or an antigenic fragment thereof (claim 15), comprising antigenic fragments of Tbp and/or Hsf like protein capable of generating a protective response against Neisserial infection (claim 16), comprising antigenic fragments of TbpA and/or Hsf (claim 17), comprising a fusion protein of Tbp and Hsf like protein or antigenic fragments thereof (claim 18), comprising a fusion protein comprising TbpA and Hsf or antigenic fragments thereof capable of generating a protective response against Neisserial infection (claim 19), further comprising plain or conjugated bacterial capsular polysaccharide or oligosaccharide (claim 45), comprising two or more bacterial capsular polysaccharides or oligosaccharides conjugated to transferrin binding protein or Hsf like proteins or both (claim 46), wherein the capsular polysaccharide or oligosaccharide is derived from one or more bacteria selected from the group consisting of Neisseria meningitidis serogroup A, Neisseria meningitidis serogroup C, Neisseria meningitidis serogroup Y, Neisseria meningitidis serogroup W-135, Haemophilus influenzae b, Streptococcus pneumoniae, Group A Streptococci, Group B Streptococci, Staphylococcus aureus and Staphylococcus" epidermidis (claim 47),

comprising an adjuvant (claim 51), comprising aluminium salts (claim 52), comprising 3D-MPL (claim 53), comprising an adjuvant containing CpG (claim 54); a vaccine comprising the immunogenic composition of claim 1 and a pharmaceutically acceptable excipient (claim 55).

Berthet et al teach a bleb vaccine comprising a genetically-engineered bleb preparation isolated from a modified *N. meningitidis B* strain wherein one ore more genes are upregulated such as Hsf-like, TbpA, and TbpB antigens (see claims 1-2, 13-14) wherein the Gram-negative bacterial strain such as *Nesseria* strain is characterized in that said preparation is obtainable by employing one or more processes such as a process of upregulating expression of protective OMP antigens within the bleb preparation comprising the steps of identifying such antigen, engineering a bacterial strain so as to introduce a stronger promoter sequence upstream of a gene encoding said antigen such that said gene is expressed at a level higher than in the non-modified bleb, and making blebs from said strain or a process of upregulating expression of protective OMP antigens within the bleb preparation comprising the steps of identifying such antigen, engineering a bacterial strain so as to introduce into the chromosome one or more further copies of a gene encoding said antigen controlled by a heterologous, stronger promoter sequence, and making blebs from said strain (see claims 1 and 2 and abstract) which correlate to an immunogenic composition an immunogenic composition comprising an isolated transferring binding protein (Tbp) or antigenic fragment thereof and an isolated Hsf like protein or antigenic fragment thereof from the same or different Gram negative bacteria.

Berthet et al teach bleb components produced conditionally and the expression of some genes coding for certain bleb components is carefully regulated. Berthet et al teach Neisserial bleb preparations one or more of the following genes (encoding protective antigens) are preferred for upregulation via processes b) and/or i) when carried out on a Neisserial strain, including gonococcus, and meningococcus (particularly N. meningitidis B), Hsf-like, TbpA, TbpB (see pg. 26 lines 1-20, pg. 27 lines 25-30, pg. 28 lines 1-15, pg. 31 lines 1-15). Berthet et al teach a genetically-engineered bleb preparation from a Gram-negative bacterial strain wherein the Gram-negative strain is Neisseria gonorrhoeae (see pg. 31 lines 1-15). Berthet et al teach the bleb preparation in the manufacture of a

medicament for immunizing a human host against a disease caused by infection of one or more of the following: Neisseria meningitidis, Neisseria gonorrhoeae. Berthet et al teach a meningitis vaccine comprising the bleb preparation of one or more plain or conjugated pneumococcal capsular polysaccharides and a meningococcal vaccine comprising the bleb preparation of one or more plain or conjugated meningococcal capsular polysaccharides selected from the serotypes A, C, Y or W (see pg 36). Berthet et al teach bleb preparations of the present invention may be adjuvant in the vaccine formulation of the invention such as aluminum salt such as aluminum hydroxide gel (alum) or aluminum phosphate, and 3-de-O-acylated monophosphoryl lipid A (3D- MPL) together with an aluminum salt (see pgs. 33-34). Berthet et al teach that unmethylated CpG containing oligo nucleotides are suitable for use in the present invention (see claims see pgs. 33-34).

Conclusion

5. No claims are allowed.

6. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a). A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nina A. Archie whose telephone number is 571-272-9938. The examiner can normally be reached on Monday-Friday 8:30-5:00p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner supervisor, Robert Mondesi can be reached on 571-272-0956. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Nina A Archie
Examiner
GAU 1645
REM 3B31

/Robert A. Zeman/

for Nina Archie, Examiner of Art Unit 1645